



hypermethioninemia

Hypermethioninemia is an excess of a particular protein building block (amino acid), called methionine, in the blood. This condition can occur when methionine is not broken down (metabolized) properly in the body.

People with hypermethioninemia often do not show any symptoms. Some individuals with hypermethioninemia exhibit intellectual disability and other neurological problems; delays in motor skills such as standing or walking; sluggishness; muscle weakness; liver problems; unusual facial features; and their breath, sweat, or urine may have a smell resembling boiled cabbage.

Hypermethioninemia can occur with other metabolic disorders, such as homocystinuria, tyrosinemia and galactosemia, which also involve the faulty breakdown of particular molecules. It can also result from liver disease or excessive dietary intake of methionine from consuming large amounts of protein or a methionine-enriched infant formula.

Frequency

Primary hypermethioninemia that is not caused by other disorders or excess methionine intake appears to be rare; only a small number of cases have been reported. The actual incidence is difficult to determine, however, since many individuals with hypermethioninemia have no symptoms.

Genetic Changes

Mutations in the *AHCY*, *GNMT*, and *MAT1A* genes cause hypermethioninemia.

Inherited hypermethioninemia that is not associated with other metabolic disorders can be caused by shortages (deficiencies) in the enzymes that break down methionine. These enzymes are produced from the *MAT1A*, *GNMT* and *AHCY* genes. The reactions involved in metabolizing methionine help supply some of the amino acids needed for protein production. These reactions are also involved in transferring methyl groups, consisting of a carbon atom and three hydrogen atoms, from one molecule to another (transmethylation), which is important in many cellular processes.

The *MAT1A* gene provides instructions for producing the enzyme methionine adenosyltransferase. This enzyme converts methionine into a compound called S-adenosylmethionine, also known as AdoMet or SAME. The *GNMT* gene provides instructions for making the enzyme glycine N-methyltransferase. This enzyme starts the next step in the process, converting AdoMet to a compound called S-adenosyl homocysteine, or AdoHcy. The *AHCY* gene provides instructions for producing the enzyme S-adenosylhomocysteine hydrolase. This enzyme converts the AdoHcy into the

compound homocysteine. Homocysteine may be converted back to methionine or into another amino acid, cysteine.

A deficiency of any of these enzymes results in a buildup of methionine in the body, and may cause signs and symptoms related to hypermethioninemia.

Inheritance Pattern

Hypermethioninemia can have different inheritance patterns. This condition is usually inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition.

Hypermethioninemia is occasionally inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In these cases, an affected person usually has one parent with the condition.

Other Names for This Condition

- Deficiency of methionine adenosyltransferase
- glycine N-methyltransferase deficiency
- GNMT deficiency
- Hepatic methionine adenosyltransferase deficiency
- MAT deficiency
- MET
- methionine adenosyltransferase deficiency
- methioninemia
- S-adenosylhomocysteine hydrolase deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Increased Methionine
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Methionine.pdf>

Genetic Testing

- Genetic Testing Registry: Glycine N-methyltransferase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1847720/>
- Genetic Testing Registry: Hepatic methionine adenosyltransferase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268621/>
- Genetic Testing Registry: Hypermethioninemia with s-adenosylhomocysteine hydrolase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3151058/>

Other Diagnosis and Management Resources

- Baby's First Test
<http://www.babysfirsttest.org/newborn-screening/conditions/hypermethioninemia>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Amino Acid Metabolism Disorders
<https://medlineplus.gov/aminoacidmetabolismdisorders.html>
- Health Topic: Genetic Brain Disorders
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Newborn Screening
<https://medlineplus.gov/newbornscreening.html>

Genetic and Rare Diseases Information Center

- Glycine N-methyltransferase deficiency
<https://rarediseases.info.nih.gov/diseases/10764/glycine-n-methyltransferase-deficiency>
- Methionine adenosyltransferase deficiency
<https://rarediseases.info.nih.gov/diseases/8397/methionine-adenosyltransferase-deficiency>

Educational Resources

- Biochemistry (fifth edition, 2002): Methionine Metabolism
<https://www.ncbi.nlm.nih.gov/books/NBK22453/?rendertype=figure&id=A3252>
- Disease InfoSearch: Hepatic methionine adenosyltransferase deficiency
<http://www.diseaseinfosearch.org/Hepatic+methionine+adenosyltransferase+deficiency/8509>
- Disease InfoSearch: Hypermethioninemia
<http://www.diseaseinfosearch.org/Hypermethioninemia/9824>
- Disease InfoSearch: Hypermethioninemia with s-adenosylhomocysteine hydrolase deficiency
<http://www.diseaseinfosearch.org/Hypermethioninemia+with+s-adenosylhomocysteine+hydrolase+deficiency/8595>
- Disease InfoSearch: Methionine adenosyl transferase deficiency
<http://www.diseaseinfosearch.org/Methionine+adenosyl+transferase+deficiency/4709>
- MalaCards: hypermethioninemia
<http://www.malacards.org/card/hypermethioninemia>
- Orphanet: Brain demyelination due to methionine adenosyltransferase deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=168598
- Orphanet: Hypermethioninemia due to glycine N-methyltransferase deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=289891
- Orphanet: Psychomotor retardation due to S-adenosylhomocysteine hydrolase deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=88618
- Screening, Technology and Research in Genetics
<http://www.newbornscreening.info/>

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases
<http://www.climb.org.uk>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22hypermethioninemia%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28hypermethioninemia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- GLYCINE N-METHYLTRANSFERASE DEFICIENCY
<http://omim.org/entry/606664>
- HYPERMETHIONINEMIA WITH S-ADENOSYLHOMOCYSTEINE HYDROLASE DEFICIENCY
<http://omim.org/entry/613752>
- METHIONINE ADENOSYLTRANSFERASE I/III DEFICIENCY
<http://omim.org/entry/250850>

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Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/hypermethioninemia>

Reviewed: April 2007

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications

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National Institutes of Health

Department of Health & Human Services